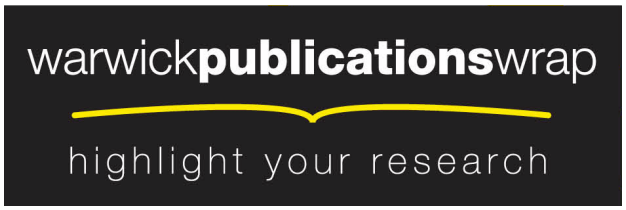

Predictors of Employment in Bipolar Disorder: a systematic review

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Abstract

Background

Severe work impairment can be present for a considerable proportion of the course of bipolar disorder (BD) and is costly for governments, services and individuals. Understanding predictors of employment in BD is therefore crucial as some may be susceptible to interventions. We conducted a systematic review of prospective studies in order to identify predictors of employment in people with BD.

Methods

We searched Medline, PsychInfo, EMBASE and Web of Science databases, hand searched 3 journals and used predetermined criteria to select papers for full text inclusion. Sixty seven papers were identified. Nine met inclusion criteria, with a total sample of 3184.

Results

Studies included in this review identified cognitive deficits (67%, n=4), depression (43%, n=3) and level of education (33%, n=2) as predictors of employment in BD patients. Bipolar depression not only affects whether someone is employed but also time off work. Even sub-syndromal depression appears to damage employment prospects. Verbal memory and executive functioning appear to be predictors of work functioning.

Limitations

Conclusions are based on a relatively small number of studies and are therefore subject to change with the addition of further studies. A formal meta-regression was not possible due

to differences between measures of employment and work functioning.

Conclusions

Better assessment and management of depression and cognitive difficulties could improve the occupational functioning of BD patients. There is a need for high quality longitudinal studies specifically designed to investigate predictors of employment in large bipolar disorder samples.

Keywords: Bipolar Disorder, Employment, Prediction, Work, Outcome

Introduction

Employment is highly valued by people with mental illness and return to work seen as integral to their notion of recovery (Dunn et al 2008). Return to employment is therefore a key outcome of treatment of whatever modality for mental illness. For mental disorders as a whole the costs of the loss of productivity associated with worklessness are more than double the actual care costs (Patel and Knapp 1998). More specifically in the US, the costs of bipolar disorder in 1991 were estimated to be $45 billion, with $38 billion of this being due to the loss of wage earning (Wyatt and Henter 1995). The socio-economic cost of bipolar disorder to UK society in 2007 was £5.2 billion (McCrone 2008). In terms of global burden of disease bipolar disorder is the 22nd highest cause of life years lost to premature mortality and years lived with disability, higher than schizophrenia or asthma (Murray and Lopez 1997) and functional losses associated with bipolar disorder are large (Judd et al 2005).

Bipolar disorder is associated with damage to employment prospects, poor work performance and absenteeism (Dean et al 2004). Despite high levels of post 16 years education, less than 50% of people with bipolar disorder living in Europe may be in paid employment (Morselli et al 2004) and 55% of bipolar patients experience financial difficulties (Calabrese et al 2003, Hirschfeld et al 2003). This is concerning, as a high proportion of those affected by bipolar disorder are young to middle-aged and would normally be expected to be economically active. For those people who are in employment, evidence suggests that problems at work are frequently encountered (Morselli et al 2004). Severe work impairment is present for a considerable proportion of the long term course of bipolar disorder (Judd et al 2008) and maintaining or returning to previous job roles is often not possible, with many

people being employed at a sub optimal level (Sanchez- Moreno et al 2009).

The substantial economic and social costs of bipolar disorder make an understanding of the predictors of employment critical but no previous systematic review has examined what these factors are. Some of these predictors of working may be susceptible to interventions, whilst others would enable a fuller understanding of those people most at risk of unemployment. Both groups of predictors are likely to be useful clinically, but also in directing future research, so that the long term employment prospects of bipolar disorder patients can be improved.

We therefore conducted a systematic review of prospective studies in order to identify predictors of employment in people with bipolar disorder. We decided to focus on the clearest and most easily understood measure of work outcome: employment rate, an objective, easily identifiable and reliable measure. As a secondary measure we also included studies that focused specifically on work functioning if this was clearly identified. We use the MOOSE (Meta-analysis Of Observational Studies in Epidemiology) guidelines (Stroup et al 2000) as a framework for reporting this systematic review.

Methods

Databases and search terms

S.M completed the main search. Medline (1950-current), PsychInfo (earliest to current), EMBASE (earliest to current) and Web of Science (1914-current) databases were searched in March 2011 for papers in the English language. Search terms were used in groups and subsequently results were amalgamated. Search terms used were: bipolar, manic

depression, affective psychosis (group 1) AND work, employment, occupation, job, vocation (group 2) AND association, predict, correlate (group 3). The reference lists of review papers were scrutinised for any relevant further studies and a hand search was carried out of published articles over the last five years of three journals that appeared to contain a significant quantity of papers in this subject area. The hand searched journals were the Journal of Affective Disorders, Bipolar Disorders and The American Journal of Psychiatry.

Initial screening of search output

We took the view that the number of papers that would provide significant results may be limited and therefore we decided on a strategy of being over-inclusive at this stage. This view was based on S.M's previous experience of conducting literature reviews on employment and schizophrenia and that there is less funded research and quantity of literature in bipolar disorder in comparison to Schizophrenia (Clement et al 2003).

Search results were downloaded into ENDNOTE X5. Titles of papers were inspected and if obviously not relevant the abstracts were not read. Subsequent to this initial screen the remaining abstracts were studied and a set of pre-agreed rules were applied in order to identify papers for full text retrieval. Abstracts were included if a) the sample comprised bipolar disorder I or II or the sample was described as having a severe mental illness b) irrespective of whether early or established cases of bipolar disorder were sampled c) they were therapeutic trials as long as the control arm was treatment as usual d) sample size was more than 15 e) the sample was prospective and f) length of follow-up was at least 6 months.

Check of reliability of paper selection

Both S.M. and E.G. independently coded 100% of the abstracts (N=279) applying the inclusion criteria for full text retrieval. S.M. coded 14 papers for inclusion that had not been identified as such by E.G. The authors met to review these discrepancies, which were mainly related to whether the study design met the criteria for full text retrieval. If there was significant doubt about whether an abstract should be included for full text retrieval we decided to include rather than exclude. After discussion 9 of the 14 discrepant papers were included. After this process 67 papers were ultimately identified for full text retrieval.

Data Extraction

All full text papers were read and, if suitable, data extracted on: sample size, proportion of people retained at follow-up, sampling frame, type of study, length of follow up, and predictors of employment rate or work functioning at each time point. Only studies that used adjusted analyses were included, with those reporting simple correlations between a variable and work being excluded. We also excluded studies that did not specifically report employment rate or work functioning.

Analysis

The nature of data extracted and the heterogeneity between studies and measures used precluded a formal meta-regression. We developed an assessment framework and assigned each paper a quality marker based on criteria. Each included study was given one star for

each of the following criterion:

a) Sample size > 100

b) Length of follow-up of at least 18 months

c) Epidemiologically representative sample i.e. systematic or probability samples as opposed to convenience sample so that the sample represents to a large extent the whole population of patients with bipolar disorder.

d) Inclusion and exclusion criteria for the sample clearly described.

e) Employment rate given. We decided to give preference to this measure compared to work functioning. It also allows meaningful comparisons to be made between studies, rather than measures of work functioning which might use widely different scales, often conflating different domains into one instrument.

Results

The initial search strategy identified 2265 abstracts; when repeats were excluded this dropped to 1673. After an initial screen of abstract titles, a total of 279 complete abstracts were read. 67 papers were selected for full text retrieval and were read, with 9 meeting the full criteria for inclusion and final data extraction. These studies sampled a total of 3184 people with bipolar disorder and the mean length of follow-up was 24.6 months. The main reasons for studies being excluded subsequent to full text retrieval were: employment or work functioning data was not given, the study design or analysis was not prospective, and the sample of bipolar disorder was not clearly defined. The review process is outlined in Figure 1.

Figure 1 about here

The studies included in the final analysis are shown in Table 1 ordered by our quality assessment.

Table one about here

Nature of studies identified

Overall there were only a small number of studies (N=9) that met our inclusion criteria despite our initial over-inclusive search strategy. Attrition rates in the included studies ranged from 4 to 39 per cent. Using our assessment of quality there were no studies rated as 5 stars, one study rated as 4 stars, two as 3 stars, two as 2 stars and four as 1 star.

Table 2 shows the percentage of studies in which individual variables were significant. Depression was the most frequently assessed individual variable in the nine included studies, although a range of different measures that could be labeled as bipolar disorder severity were also commonly investigated. Focusing on variables that were examined in at least five of the nine studies, the highest signal strength appeared to be for cognitive factors, depression and education. 67% of studies that investigated them found cognitive factors to be statistically important in predicting employment rate or work functioning. The respective figures for depression and education were 43% and 33%.

Table 2 about here

Socio-demographic predictors

Socio-demographic factors were associated with employment status or work functioning in three studies, one of which used employment rate as the main outcome measure. A multi-centre study by Gilbert et al (2010) found that those bipolar patients who had not completed high school were less likely to be employed, volunteering or carrying out a full time homemaker role at follow-up. This relationship between educational attainment and work impairment was also reported in another moderate quality study (Reed et al 2010) based on a much larger sample of bipolar patients. Lower educational attainment predicted high work impairment at both the primary education vs. university and the secondary education vs. university levels. Four further studies that examined the predictive role of educational attainment did not support these findings.

An association between additional socio-demographic variables was also found; Reed et al (2010) reported that patients living in a relationship with someone or living in independent housing were less likely to have high work impairment at the two year follow-up point. These findings were consistent with those of Hammen et al (2000) who reported that better social functioning as rated by a psychiatrist (including relationship functioning) predicted better work functioning on the Work Adjustment Scale.

Affective symptom predictors

Affective episodes were frequently explored as explanatory factors predicting employment in this review. Four of the 9 studies that met inclusion criteria described a statistically significant relationship with depression or mania. Depression was identified as a predictor of

employment in 3 studies (Simon et al 2008, Bonnin et al 2010, Burdick et al 2010) including those that we rated as being of higher quality, but was not found to be significant in 4 others.

Simon et al (2008) found that a major depressive episode at any time point over 24 months was associated with lower probability of being in full time employment. The length of the depressive episode also predicted employment status with those who were unemployed at the 12 month follow-up experiencing 50% more weeks in a depressive episode in the prior year than those who were employed. Each additional week of a major depressive episode was associated with a 5% lower likelihood of paid employment at the 12 month follow-up point.

Depression also seemed to be important in those studies that used work functioning as opposed to employment rate as the outcome variable. Bonnin et al (2010) also reported depression as a predictor of occupational functioning derived from the Functioning Assessment Short Test (Rosa et al 2007) as opposed to employment rates. Higher scores on the Hamilton Rating Scale for Depression (HDRS, Hamilton 1960) at baseline were associated with lower occupational functioning scores in this sample at follow-up. One of the studies (Burdick et al 2010) which we rated as 1 star also supported these findings, identifying recent depression as being predictive of lower scores on the Strauss Carpenter work outcome scale (Strauss and Carpenter 1972).

Only 1 out of the 4 studies that investigated it found that manic symptoms predicted employment outcome. However within this study (Reed et al 2010) mania severity was assessed through the Clinical Global Impression scale (CGI) (Spearing et al 1997) as opposed

to a diagnostic assessment for mania. Simon et al (2008) also reported that the number of weeks spent in sub-threshold mania (but not mania) was associated with a 2% lower likelihood of employment.

Three studies scoring 1 or 2 stars reported a range of clinical characteristics other than depression or mania that were associated with employment or work functioning. Burdick et al (2010) found that the number of lifetime hospitalizations predicted lower scores on the Strauss Carpenter work outcome scale. However 3 further studies that examined the role of hospitalization did not support this finding. Substance abuse at baseline was reported to predict employment status 6 months after discharge from hospital (Dickerson et al 2010) with patients having co-morbid substance misuse less likely to be in the working group. This finding was not supported by Reed et al (2010).

Stressful life events in the previous 3 months were reported to predict delayed recovery in the work functioning domain of the Life Functioning Questionnaire (Yan-Meier et al 2011) but again this was not supported by another investigation (Hammen et al 2000). Severity of bipolar disorder was reported as being predictive of work impairment (Reed et al 2010) with high overall severity in the prior 12 months being associated with higher work impairment at follow-up as was rapid cycling.

Cognitive predictors

That cognitive deficit may play a role in predicting employment status was supported by 4 out of the 6 studies that examined this relationship. One of the higher quality studies (Gilbert et

al 2010) found that self-reported cognitive impairment at baseline increased the chances of not working at both baseline and follow-up, although the numbers in this analysis were very small. A study using neurocognitive tests (Bonnin et al 2009) found that high scores on the Digits Backwards test (Weschler 1955) were found to be predictive of lower occupational functioning, although employment rates were not given in this study.

Two other studies reporting cognitive predictors of employment were both rated by us as 1 star, with small bipolar disorder samples (mean 38) and neither of them reported employment rates. Verbal learning and memory as rated by the California Verbal Learning Test (CVLT) (Delis et al 1987) were found by Burdick et al (2010) to predict higher scores on the Strauss Carpenter work outcome scale. The executive/reasoning scale independently predicted low or good occupational adaptation in this study. Composite neurocognitive scores at baseline were found by Tabares-Seisdedos et al (2008) to predict good or low occupational adaptation group membership at follow-up, and that the executive/reasoning domain of the measured neurocognitive domains predicted membership of the "good" or "low" occupational adaptation group.

Discussion

To our knowledge this is the first systematic review of predictors of employment in people with bipolar disorder.

Overall quality of studies found

Much of the evidence in the studies comes from samples collected for other purposes, which may explain why there were few studies rated by us as offering high quality evidence

in this area. Seven out of the 9 studies followed up patients for 2 years or less so that insights into predictors of employment in bipolar disorder patients in the longer term need strengthening. However at least some findings from the longer follow-up studies (Burdick et al 2010, Bonnin et al 2010) particularly with regards to depression were supported by studies that followed up patients for a shorter period. For example Simon et al (2008) reported recent or current depression as a predictor of low work functioning or unemployment. Measures of cognitive functioning varied between studies and there was little replication in assessing the effects of different aspects of cognition amongst the studies found.

Samples were small (less than 100) in two thirds of the studies and there was minimal differentiation of the different types of bipolar disorders, making it impossible for us to comment on whether the same predictors of employment exist in bipolar I or II patients.

Only 3 of the 9 included studies reported our preferred measure of employment rate as opposed to a measure of work functioning. A number of different instruments were used to determine work functioning including the Strauss-Carpenter Work Adjustment Scale, the Modified Vocational Status Index (Tohen et al 2000) and the work functioning dimensions of other global functioning scales. None of the studies that used work functioning used the same measure and this variety makes comparison of results problematic given that points on different scales would not normally or necessarily represent equivalent functioning. This anticipated difficulty with the literature validated our decision to focus on employment rates. Employment rates ranged from 61-75% (mean 66%) at follow-up. However, variations in definition of “employed” were apparent even within these 3 studies with one study combining students with part-time workers.

Socio-demographic predictors

Educational attainment was reported in one study as a predictor of employment rate at both baseline and at follow up, and in another study as a predictor of work functioning. It would seem reasonable that education would have an impact on occupational status in the bipolar disorder population in the same way that it does in the wider population. Work history was used as a baseline measure in only 1 study included in this review (Dickerson 2010). This is surprising as in the schizophrenia literature work history seems to be the strongest predictor of future employment (Marwaha & Johnson 2004). It is difficult to say whether many of the factors found in this review to be important in predicting employment would remain so if job history were controlled for in the analyses.

The role that close relationships and housing play in protecting bipolar disorder patients from impairments in work functioning is unclear. Ability to make close relationships suggests good interpersonal skills and this is certainly an attribute that is required to be successful in most western economies which tend to be service orientated. It may be that there is interplay between socio-demographic factors and illness severity, in that those who are able to maintain close relationships and independent housing are less severely ill or ill for shorter periods than those who cannot maintain these social circumstances.

Depression

In the studies that reported affective symptoms as predictors of employment in the bipolar population the presence of depressive symptoms was the most frequently cited factor. Depressive symptoms within bipolar disorder appear to be linked to functional difficulties particularly highly (Rosa et al 2009). This seems to be the case specifically in relation to

employment as it is with other forms of functioning, such as independent living and social functioning (Goodwin and Jamison 1990, Romans and McPherson 1992). Our findings are in line with existing evidence relating to unipolar depression, which has been shown to have a detrimental effect on education, absenteeism, presenteeism, and employment (Lerner et al. 2004).

The greater the level of depression, the greater the damage there appears to be to employment prospects. When depressive symptoms are at sub-syndromal levels the effect on employment outcome is still apparent (Simon 2008), highlighting the need for ongoing monitoring and treatment of depression in patients who do not have obvious major depression. As severity increases there is not only a lower likelihood of employment but also days missed from work due to illness. This effect is enhanced the longer the period of depression lasts and is greater than for patients with unipolar depression (Bonin et al 2010, Simon et al 2008).

Cognitive factors

Despite indications that people with bipolar disorder experience significant neurocognitive impairment both in the short and longer term (Martinez-Aran 2004, Robinson 2006, Malhi 2007) evidence from prospective studies that this impairment is predictive of employment outcome was relatively sparse. Recent studies have linked work disability in bipolar disorder with cognitive deficits (Dickerson 2004, Huxley and Baldessarini 2007). It may be that work impairment is reflected in the drift from higher to lower skilled employment so that some

people with bipolar disorder who are working are not employed at previous levels (Carlson et al 1974, Coryell et al 1993).

There is some overlap in this review with the findings of a review of the effects of cognitive difficulties in Schizophrenia conducted by Green et al (2000), which reported that aspects of neurocognition such as verbal memory, immediate memory and executive functioning are related to functional outcome. Studies that examined neurocognitive factors in this review also reported that for people with bipolar disorder, verbal learning and memory and executive functioning are predictors of work functioning or employment outcome. These cognitive abilities are related to learning new tasks, acting purposefully and making decisions, all skills that are likely to be necessary to complete most forms of employment.

Other clinical factors

Other factors predictive of occupational outcome such as rapid cycling, substance abuse, severity of illness and high CGI-Mania scores and sub-threshold mania were each identified by only a single study. The presence of or treatment for psychosis was not found to be a significant predictor in the two studies that examined this factor. There remains a need for additional research into the role that these illness factors may play in work functioning or employment prospects. Various studies included age, age of illness onset, ethnicity and gender in their analyses. These variables were not found to be significant predictors of employment outcome in any of the studies included in this review.

Limitations of this review

We were over-inclusive in our search strategy making it likely we would have obtained relevant available papers that could answer our review question. We searched four relevant databases and hand searched an additional three journals. Even with this strategy we ultimately found a relatively small number of studies to base our conclusions on, despite the importance of employment as an outcome measure to patients, services and governments. This makes our conclusions subject to change with the addition of even a relatively small number of studies.

We were unable to include studies not in the English language as we did not have translation resources. However this may have limited the extent of the geographical spread of the studies found. It is possible that publication bias may have played a part in our results although we have no evidence that it did. It may be that although employment rate is routinely collected as an outcome measure it is not the main focus of studies designed to examine other aspects of bipolar disorder and is therefore under-reported in published studies.

The method of variable entry in statistical modelling used by individual researchers were not scrutinised in this review. Neither did we use this as a marker of quality of the studies. It was also not possible to conduct a meta-regression due to a lack of standardization of data between papers and we were therefore not able to calculate a mean strength of association between the significant predictors and employment or work functioning outcomes. Whilst we present the percentage of studies in which individual factors were significant predictors of

employment, grouping of large numbers of variables from multiple studies into a smaller number of categories inevitably lacks precision.

Clinical implications

Clinical factors that predict employment in people with bipolar disorder such as depression and cognitive deficits are likely to be more amenable to intervention by psychiatrists and other mental health professionals than the more static socio-demographic variables such as such as level of education or relationship status.

There is evidence that depression in bipolar disorder plays a significant role in the occupational outcome of patients even when present at sub-syndromal levels. Although a challenge, better identification and treatment of this depression should lead to a reduction of the occupational damage being caused. Secondly cognitive deficits that appear to sit alongside bipolar disorder also reduced the chances that people will be able to work. Investigations of cognitive remediation in schizophrenia (Wykes et al 2007, Tomas et al 2010) are ongoing, but this may also be an avenue of further worthwhile enquiry in bipolar disorder. The effects of some psychotropic medications used in bipolar disorder may worsen cognitive deficits (Goldberg and Chengappa 2009) and in turn this may further damage a person's ability to work. This needs to be borne in mind when selecting pharmacological treatments.

In the UK the Equality Act 2010 is designed to protect people from disability discrimination. It is important that depression and cognitive deficits resulting from bipolar disorder are given the same consideration as perhaps more visually obvious disabilities in relation to

discrimination in the employment market. The UK act, as well as similar legislation in Europe and the US suggests employers make reasonable adjustments to enable people to obtain and continue to work. Depression and cognitive difficulties may mean more time is necessary for tasks to be completed or job roles might need to be changed. This is likely to be particularly important during economic recession when there is increased competition for significantly fewer jobs.

Research implications

Although we have been able to draw some conclusions from this review the available literature is sparse as this is a relatively new area of research with only 1 paper included in the review published prior to 2008. Sample sizes are generally small and discrimination between bipolar I and II patients is lacking. There is a clear need for further high quality longitudinal studies that are specifically designed to investigate predictors of employment in large samples of bipolar disorder patients. Factors such as psychotic symptoms and substance misuse are understudied.

Studies using employment rate as an outcome measure would be particularly beneficial as this would facilitate comparison of findings. A more consistent approach to instrument selection in future studies investigating levels of occupational functioning should also be welcomed for the same reason.

Whilst this review was only concerned with prospective studies the bi-directional relationship between work and mental health makes caution necessary in reaching firm conclusions about

predictors of employment in bipolar disorder. Moving from employment to unemployment can have a negative impact on mental health (OECD 2008, Karsten and Moser 2009) and mental health problems may make it more difficult for a person to obtain or maintain earnings at previous levels (Levinson et al 2010). The direction of causality issue needs to be further explored given the robust literature base that work history predicts future employment outcome in other severe mental illness. Future studies that examine the effects of cognitive factors, depression and education as well as other variables in bipolar disorder also need to control for job history in order to clarify whether these factors remain significant.

In this review we have focused on work outcome in terms of employment rate or work functioning. There is however a need for future research to explore other dimensions of work outcome, such as level of employment, performance at work (absenteeism / presenteeism), under employment and work ability and how these are affected in people with bipolar disorder.

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Table 1: Predictors of Employment in people with Bipolar Disorder

Authors/ Quality stars	Sample Size At baseline At follow-up	Type of study design	Sampling frame	Length of FU (yrs)	Factors associated with Employment or work functioning	Test Statistic
Gilbert et al 2010 4 (a,b,d,e)	154 148 (96%)	Longitudinal multi-centre open effectiveness trial	DSM Bipolar I	15-43 months	Dependent variable: not working Self report cognitive impairment Less than high school education CGI score (depression, mania, overall score) Clinical status (recovered/recovering), sub-threshold mania, mania, sub-threshold mixed, mixed, sub-threshold depression, depression	 OR: 2.51 OR: 0.55 NS NS
Simon et al 2008 3 (a,b,e)	441 353 at follow-up (80%)	Longitudinal	Bipolar disorder type 1 or 11 Mental health clinic outpatients (USA)	24 months	Current major depressive episode associated with 15% lower probability of employment Each additional week in a major depressive episode was associated with a 5% lower likelihood of paid employment at 12 months Each additional week in sub-threshold mania was associated with a 2% lower likelihood of paid employment at 12 months Mania/hypomania	OR: 0.84 OR: 0.942 OR: 0.977 NS
Reed et al 2010 3 (a,b,c)	2289 1398 at follow-up (61%)	Prospective observational study	Inpatients or outpatients with manic/mixed episode, 14	24 months	Dependent variable higher work impairment Low education Primary vs. university Secondary vs. university High work impairment at baseline	 OR: 2.00 OR: 1.69 OR: 1.98

			European countries		Rapid cycling CGI-BP severity CGI-BP Mania Duration of admissions in last 12 months Living together Independent housing Depression (CGI) Episode type Number of admissions previous 12 months Alcohol/drug use	OR: 1.70 OR: 1.15 OR: 1.16 OR: 1.01 OR: 0.59 OR: 0.73 NS NS NS NS
Bonnin et al 2009 2 (b, d)	32	Cohort Excluded axis 1 comorbidity	From Barcelona bipolar disorders program	Average 4.2 years	Work functioning /Functioning Assessment Short Test Depression Digit backwards (higher score lower disability) Number of affective episodes Mania Cognitive variables (executive functions, verbal fluency, attention, verbal learning and memory) Hospitalisations Occupation and educational level	 Beta 0.435 Beta 0.347 NS NS NS NS NS
Dickerson et al 2010 2 (d,e)	75 at baseline 52 at follow-up (69%)	Prospective longitudinal cohort study	Hospital admission early in illness course to inpatient or day hospital	6 months post discharge	Modified Vocational Index Full time employment / student status inversely predicted by substance misuse at baseline (only significant variable) Education	LR of model=20.69 NS

			programs. Bipolar I, II or not specified.		Cognitive variables (verbal memory, executive functioning, visual memory, verbal fluency, processing speed, visual spatial abilities)	NS
Yan-Meier et al 2011 1 (d)	65 (100%)	Longitudinal	Hospital admissions, outpatient clinic, community clinics and private practice.	15 months	Life Functioning Questionnaire (workplace/school domain) Delayed recovery in work/school functioning domain was significantly associated with one or more stressors in the previous 3 months	 OR: 7.93
Hammen et al 2000 1 (b)	52	2 year longitudinal study	Bipolar I patients receiving outpatient treatment in affective disorders clinic	2 yrs	Work adjustment scale (0-5). Higher rating indicating higher functioning. Social functioning (including ,relationship functioning) predicted better work functioning at follow up Hospitalisations Education Stress Symptom score (depression/mania severity in past year)	 No odds ratio or Beta given NS NS NS NS
Burdick et al 2010 1 (b)	33	Prospective study	Index hospitalization	15 years	Strauss Carpenter work outcome scale. CVLT (verbal learning and memory) total learning Recent depression Number of lifetime hospitalisation Cognitive (verbal fluency, executive function, accessing general knowledge) Duration of illness	 Beta 0.34 Beta -0.38 Beta - 0.44 NS NS

Tabares-Seisdedos et al 2008 1 (d)	49 43 (88%)	Longitudinal	Outpatient units (Spain)	12 months	Occupational adaptation: Executive/reasoning domain at baseline predicted membership of the “good” or “low” occupational adaptation group Chronicity of illness Hospitalisations Education Depression	 No odds ratio given. NS NS NS NS

Quality rating a) Sample size > 100; b) Length of follow-up of at least 18 months ; c) Epidemiologically representative sample ; d) Inclusion and exclusion criteria clearly described ; e) Employment rate given.

LR: Liklihood ratio, NS= not significant

Table 2: Percentage of studies in which variables were significant

Significant variable	**Percentage of studies where variable was significant**
Cognitive factors	67 (n= 4/6)
Depression	43 (n= 3/7)
Education	33 (n=2/6)
BD illness characteristics / severity (e.g. duration, episode number, composite symptom scores)	17 (n= 1/7)
Number of admissions	25 (n=1/4)
Mania	25 (n=1/4)
Duration of admission	50 (n=1/2)
Social functioning	100 (n=2/2)
Stress	50 (n=1/2)
Substance abuse	50 (n= 1/2)
Independent housing	100 (n= 1/1)
Sub-threshold mania	100 (n= 1/1)
Sub-threshold depression	100 (n= 1/1)

Figure 1: Flow diagram of review process